***Francisella tularensis* Cyclooxygenase-2**

**\*RefSeq#:** **NP\_000954**

**\*Organism (including strain): *Francisella tularensis***

**Etiologic Risk Group: Class A “Select Agent”**

**\*Disease Information (sort of like the Intro to your Mini-up): *Francisella tularensis* is a pathogenic species of Gram-negative bacteria and the causative agent of**[**tularemia**](http://en.wikipedia.org/wiki/Tularemia)**, the pneumonic form of which is often lethal without treatment. It is a fastidious, facultative**[**intracellular**](http://en.wikipedia.org/wiki/Intracellular)**bacterium which requires**[**cysteine**](http://en.wikipedia.org/wiki/Cysteine)**for growth.**[**[1]**](http://en.wikipedia.org/wiki/Francisella_tularensis#cite_note-Sherris-1)**Due to its low infectious dose, ease of spread by aerosol and high**[**virulence**](http://en.wikipedia.org/wiki/Virulence)**, *F. tularensis* is classified as a Class A Select Agent by the U.S. government, along with other potential agents of bioterrorism such as**[**Yersinia pestis**](http://en.wikipedia.org/wiki/Yersinia_pestis)**, Smallpox and Ebola.**

**Link to TDR Targets page (if present):** [**http://www.bindingdb.org/bind/luceneResult.jsp?thisInput=cyclooxygenase-2&submit=Go**](http://www.bindingdb.org/bind/luceneResult.jsp?thisInput=cyclooxygenase-2&submit=Go)

**Link to Gene Database page (NCBI, EuPath databases -e.g. TryTryp, PlasmoDB, etc - or PATRIC, etc.):**

[**http://www.ncbi.nlm.nih.gov/protein/3MDL\_A**](http://www.ncbi.nlm.nih.gov/protein/3MDL_A)

**Essentiality of this protein:**

**Target Enzyme:**

**Cyclooxygenase (COX), officially known as prostaglandin-endoperoxide synthase (PTGS):**

**Why?**

**“Francisella tularensis, a bacterium which causes tularemia in humans, is classified as a CDC category A bioterrorism agent. In this study, we demonstrate that celecoxib, an anti-inflammatory cyclooxygenase-2 inhibitor in clinical use, exhibits activity against a type A strain of F. tularensis (Schu S4), the live vaccine strain of F. tularensis (a type B strain), and F. novicida (“F. tularensis subsp. novicida”) directly in growth medium. This bacterial killing, however, was not noted with rofecoxib, despite its higher potency than that of celecoxib in inhibiting cyclooxygenase-2. The unique ability of celecoxib to inhibit the proliferation of F. tularensis could be pharmacologically exploited to develop novel anti-Francisellatherapeutic agents, of which the proof of principle is demonstrated by compound 20, a celecoxib derivative identified through the screening of a celecoxib-based focused compound library. Compound 20 inhibited the intracellular proliferation of Francisella in macrophages without causing appreciable toxicity to these host cells. Together, these data support the translational potential of compound 20 for the further development of novel, potent anti-Francisella agents.”**

[**http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2704645/**](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2704645/)

**Complex of proteins?:**  
**Druggable Target (list number or cite evidence from a paper/database showing druggable in another organism):**  
**See “Essentiality of Protein” section, the target can be drugged/attached to. Also see:** [**http://www.bindingdb.org/bind/luceneResult.jsp?thisInput=cyclooxygenase-2&submit=Go**](http://www.bindingdb.org/bind/luceneResult.jsp?thisInput=cyclooxygenase-2&submit=Go)

**\*EC#:1.14.99.1**

**Link to BRENDA EC# page: Brenda Info:**

[**http://brenda-enzymes.org/php/result\_flat.php4?ecno=1.14.99.1**](http://brenda-enzymes.org/php/result_flat.php4?ecno=1.14.99.1)

|  |  |
| --- | --- |
| **Reaction catalyzed by prostaglandin-endoperoxide synthase (1.14.99.1)** |  |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | + |  | [AH2](javascript:MolPicture('25117')" \o "magnify and open a search engine for compound picture) | + | 2 |  | = |  |  | + |  | [A](javascript:MolPicture('26977')" \o "magnify and open a search engine for compound picture) | + |  | [H2O](javascript:MolPicture('27493')" \o "magnify and open a search engine for compound picture) |
|  | [arachidonate](javascript:MolPicture('7113')" \o "magnify and open a search engine for compound picture) | + |  | [AH2](javascript:MolPicture('25117')" \o "magnify and open a search engine for compound picture) | + |  | [2 O2](javascript:MolPicture('14738')" \o "magnify and open a search engine for compound picture) | = |  | [prostaglandin H2](javascript:MolPicture('15885')" \o "magnify and open a search engine for compound picture) | + |  | [A](javascript:MolPicture('26977')" \o "magnify and open a search engine for compound picture) | + |  | [H2O](javascript:MolPict%EF%BF%BDre('27493')" \o "magnify and open a search engine for compound picture) |

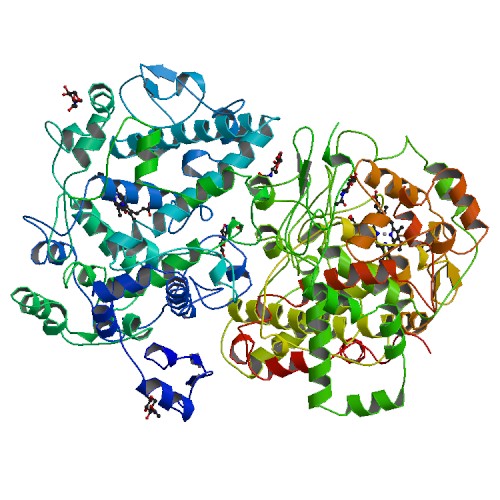
**Structure (PDB or Homology model)**  
-- PDB # or closest PDB entry if using homology model:  
-- For Homology Model option:  
---- Show pairwise alignment of your BLASTP search in NCBI against the PDB  
---- Query Coverage:  
---- Max % Identities:  
---- % Positives  
---- Chain used for homology:

**Current Inhibitors:**

**Expression Information (has it been expressed in bacterial cells):**

**Purification Method:**

**Image of protein (PyMol with features delineated and shown separately):**

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**\*Amino Acid Sequence (paste as text only - not as screenshot or as 'code'):**

**Protein Sequence- FASTA:**

**>5COX:A|PDBID|CHAIN|SEQUENCE**

**ANPCCSNPCQNRGECMSTGFDQYKCDCTRTGFYGENCTTPEFLTRIKLLLKPTPNTVHYILTHFKGVWNIVNNIPFLRSL**

**IMKYVLTSRSYLIDSPPTYNVHYGYKSWEAFSNLSYYTRALPPVADDCPTPMGVKGNKELPDSKEVLEKVLLRREFIPDP**

**QGSNMMFAFFAQHFTHQFFKTDHKRGPGFTRGLGHGVDLNHIYGETLDRQHKLRLFKDGKLKYQVIGGEVYPPTVKDTQV**

**EMIYPPHIPENLQFAVGQEVFGLVPGLMMYATIWLREHQRVCDILKQEHPEWGDEQLFQTSKLILIGETIKIVIEDYVQH**

**LSGYHFKLKFDPELLFNQQFQYQNRIASEFNTLYHWHPLLPDTFNIEDQEYSFKQFLYNNSILLEHGLTQFVESFTRQIA**

**GRVAGGRNVPIAVQAVAKASIDQSREMKYQSLNEYRKRFSLKPYTSFEELTGEKEMAAELKALYSDIDVMELYPALLVEK**

**PRPDAIFGETMVELGAPFSLKGLMGNPICSPQYWKPSTFGGEVGFKIINTASIQSLICNNVKGCPFTSFNVQDPQPTKTA**

**TINASASHSRLDDINPTVLIKRRSTEL**

**>5COX:B|PDBID|CHAIN|SEQUENCE**

**ANPCCSNPCQNRGECMSTGFDQYKCDCTRTGFYGENCTTPEFLTRIKLLLKPTPNTVHYILTHFKGVWNIVNNIPFLRSL**

**IMKYVLTSRSYLIDSPPTYNVHYGYKSWEAFSNLSYYTRALPPVADDCPTPMGVKGNKELPDSKEVLEKVLLRREFIPDP**

**QGSNMMFAFFAQHFTHQFFKTDHKRGPGFTRGLGHGVDLNHIYGETLDRQHKLRLFKDGKLKYQVIGGEVYPPTVKDTQV**

**EMIYPPHIPENLQFAVGQEVFGLVPGLMMYATIWLREHQRVCDILKQEHPEWGDEQLFQTSKLILIGETIKIVIEDYVQH**

**LSGYHFKLKFDPELLFNQQFQYQNRIASEFNTLYHWHPLLPDTFNIEDQEYSFKQFLYNNSILLEHGLTQFVESFTRQIA**

**GRVAGGRNVPIAVQAVAKASIDQSREMKYQSLNEYRKRFSLKPYTSFEELTGEKEMAAELKALYSDIDVMELYPALLVEK**

**PRPDAIFGETMVELGAPFSLKGLMGNPICSPQYWKPSTFGGEVGFKIINTASIQSLICNNVKGCPFTSFNVQDPQPTKTA**

**TINASASHSRLDDINPTVLIKRRSTEL**

**>5COX:C|PDBID|CHAIN|SEQUENCE**

**ANPCCSNPCQNRGECMSTGFDQYKCDCTRTGFYGENCTTPEFLTRIKLLLKPTPNTVHYILTHFKGVWNIVNNIPFLRSL**

**IMKYVLTSRSYLIDSPPTYNVHYGYKSWEAFSNLSYYTRALPPVADDCPTPMGVKGNKELPDSKEVLEKVLLRREFIPDP**

**QGSNMMFAFFAQHFTHQFFKTDHKRGPGFTRGLGHGVDLNHIYGETLDRQHKLRLFKDGKLKYQVIGGEVYPPTVKDTQV**

**EMIYPPHIPENLQFAVGQEVFGLVPGLMMYATIWLREHQRVCDILKQEHPEWGDEQLFQTSKLILIGETIKIVIEDYVQH**

**LSGYHFKLKFDPELLFNQQFQYQNRIASEFNTLYHWHPLLPDTFNIEDQEYSFKQFLYNNSILLEHGLTQFVESFTRQIA**

**GRVAGGRNVPIAVQAVAKASIDQSREMKYQSLNEYRKRFSLKPYTSFEELTGEKEMAAELKALYSDIDVMELYPALLVEK**

**PRPDAIFGETMVELGAPFSLKGLMGNPICSPQYWKPSTFGGEVGFKIINTASIQSLICNNVKGCPFTSFNVQDPQPTKTA**

**TINASASHSRLDDINPTVLIKRRSTEL**

**>5COX:D|PDBID|CHAIN|SEQUENCE**

**ANPCCSNPCQNRGECMSTGFDQYKCDCTRTGFYGENCTTPEFLTRIKLLLKPTPNTVHYILTHFKGVWNIVNNIPFLRSL**

**IMKYVLTSRSYLIDSPPTYNVHYGYKSWEAFSNLSYYTRALPPVADDCPTPMGVKGNKELPDSKEVLEKVLLRREFIPDP**

**QGSNMMFAFFAQHFTHQFFKTDHKRGPGFTRGLGHGVDLNHIYGETLDRQHKLRLFKDGKLKYQVIGGEVYPPTVKDTQV**

**EMIYPPHIPENLQFAVGQEVFGLVPGLMMYATIWLREHQRVCDILKQEHPEWGDEQLFQTSKLILIGETIKIVIEDYVQH**

**LSGYHFKLKFDPELLFNQQFQYQNRIASEFNTLYHWHPLLPDTFNIEDQEYSFKQFLYNNSILLEHGLTQFVESFTRQIA**

**GRVAGGRNVPIAVQAVAKASIDQSREMKYQSLNEYRKRFSLKPYTSFEELTGEKEMAAELKALYSDIDVMELYPALLVEK**

**PRPDAIFGETMVELGAPFSLKGLMGNPICSPQYWKPSTFGGEVGFKIINTASIQSLICNNVKGCPFTSFNVQDPQPTKTA**

**TINASASHSRLDDINPTVLIKRRSTEL**

**\*length of your protein in Amino Acids**: **587**

**Weight of Protein:** **274398.11**

**\*CDS Gene Sequence (paste as text only):**

**\*GC% Content for gene:**

**\*CDS Gene Sequence (codon optimized) - copy from output of Primer Design Protocol (paste as text only):**

**\*GC% Content for gene (codon optimized):**

**Primer design results for pNIC-Bsa4 cloning (list seqeunces of all of your ~40 nt long primers):**  
**(link to DNA Works output text file -**that should be saved in your Google Docs folder after you did the primer design protocol)  
-- Ask a mentor, Dr. B, or a fellow researcher -how to link a GDocs file if you are not sure how to.

**Primer design results for 'tail' primers (this is just 2 sequences):**  
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**Resources:**

See **ProtocolTargetDiscoveryVDS.docx** for more  
Etiologic Risk Group Categories (for pathogens): <http://www.utexas.edu/research/rsc/ibc/agent_class.html#_Toc7238334>  
  
**SIGMA-ALDRICH RESOURCES**  
Enzyme Explorer  
<http://www.sigmaaldrich.com/life-science/metabolomics/enzyme-explorer.html>  
  
Enzyme Classification Index (EC number)  
<http://www.sigmaaldrich.com/life-science/biochemicals/biochemical-products.html?TablePage=14573088>  
  
  
WolframAlpha <http://www.wolframalpha.com/>  
DrugBank <http://www.drugbank.ca/>  
  
  
**Databases of genes/organisms:**  
<http://www.niaid.nih.gov/Pages/default.aspx>  
<http://eupathdb.org/eupathdb/>  
<https://patricbrc.vbi.vt.edu/portal/portal/patric/Home>  
<http://www.nmpdr.org/FIG/wiki/view.cgi/Main/EssentialGenes>  
<http://tubic.tju.edu.cn/deg/>  
<http://csgid.org/csgid/cake/pages/community_request_gateway>  
<http://tdrtargets.org/>  
<http://gsc.jcvi.org/status.shtml>  
  
  
**Scientific Nomenclature page from Center for Disease Control (gene, protein names and abbreviations)**  
<http://wwwnc.cdc.gov/eid/pages/scientific-nomenclature.htm>  
  
  
**Gene Information:**  
NCBI GENE Page: <http://www.ncbi.nlm.nih.gov/gene>  
BLAST Page: <http://blast.ncbi.nlm.nih.gov/>  
  
**Protein Information:**  
NCBI Protein Page: <http://www.ncbi.nlm.nih.gov/protein>  
[Protein Expression Website](http://www.embl.de/pepcore/pepcore_services/protein_expression/ecoli/index.html)  
Protein Expression Paper: [SGC\_ProteinProductionPurificationNatMethods2008.pdf](http://vdsstream.wikispaces.com/file/view/SGC_ProteinProductionPurificationNatMethods2008.pdf/318880426/SGC_ProteinProductionPurificationNatMethods2008.pdf)  
  
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[StemmerPCRoverlapGene1995.pdf](http://vdsstream.wikispaces.com/file/view/StemmerPCRoverlapGene1995.pdf/256805234/StemmerPCRoverlapGene1995.pdf)  
  
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